## REMARKS/ARGUMENTS

### Claim Status/Support For Claim Amendment

In response to the Office Action of April 7, 2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim 1 has been amended. Claims 2-35 have been cancelled. Claims 36-43 have been added. Claims 1 and 36-43 are pending in the instant application.

No new matter has been added by the addition of new claims 36-43. The subject matter of new claims 36-43 corresponds to the subject matter of canceled claims 2-35. The above additions to the claims also find basis in the original disclosure at page 12, lines 2-12; page 17, lines 7-14; page 18, lines 5-7 and page 27, line 17 to page 28, line 2. The method of claims 36-40 is described in detail at pages 20-27. Page 28,line 11 to page 29,line 7 refers to the use of various types of samples and their measurement. Figure 1 shows data derived when using the claimed method on samples obtained from a human patient. Page 28, line 3 to page 33, line 2 describes kits and their contents contemplated for use with the claimed methods. It is clear from these specific recitations and from the description of methods utilized that the methods and types of kits were fully contemplated by the inventors at the time of filing and were enabled by virtue of the disclosure as originally filed.

**Restriction/Election**

Considering that new claims 36-43 are limited to the use of a peptide consisting of SEQ ID NO:1, a search of these claims would encompass this specific peptide. As was mentioned in the Response filed on February 4, 2003, the instant application is related, in claim format, to several other pending applications. In an effort to maintain equivalent scope in these applications, Applicants would appreciate the Examiner's reconsideration of the restriction requirement in light of the overlapping search and rejoin under *Ochai* claim 1 which is drawn to a specific peptide to claims 36-43 which are drawn to methods and kits limited to use of the specific peptide of claim 1. If SEQ ID NO:1 is found to be novel, then methods and kits limited to its use should also be found novel.

**Objections to the Drawings**

At page 3, of the Office Action mailed on April 7, 2003, the Examiner objected to the drawings under 37 CFR 1.821(a)(1) and 1.821(a)(2) because the drawings contain sequences which have not been identified appropriately with a SEQ ID NO.

According to MPEP 2422.02, the sequence identifier for sequences present in the drawings must be used either in the drawing itself or in the Brief Description of the Drawings. Applicants have herein amended the specification at the Brief Description of the Drawings section to include sequence identifiers

for all sequences included in the drawings. Thus, Applicants respectfully submit that the drawings are now in compliance with 37 CFR 1.821(a)(1) and 1.821(a)(2) and request that the objections to the drawings now be withdrawn.

**Sequence Compliance**

At page 4 of the Office Action mailed on April 7, 2003, the Examiner objected to the application under 37 CFR 1.821(a)(1) through 1.825 because the application contains sequences which have not been identified appropriately with a SEQ ID NO. The Examiner indicates that a form, "Notice To Comply" was attached to the Office Action, however Applicants did not find such form attached.

Applicants have reviewed the entire specification including the figures and the claims for sequence disclosures. The only sequence found to be disclosed is the amino acid sequence identified as SEQ ID NO:1. Applicants have herein amended the specification at the Brief Description of the Drawings section to include sequence identifiers for all sequences included in the drawings. The claims and the specification (at page 27, line 18) were amended to include the proper sequence identification numbers in the Supplemental Preliminary Amendment filed on April 23, 2002. Applicants respectfully submit that the application is now in compliance with 37 CFR 1.821(a)(1) through 1.825 and request that this objection now be withdrawn.

**Objections to the Specification**

I. The Examiner indicated a typographical error at page 6, line 13 of the specification. Applicants have herein amended the specification to correct this typographical error. Applicants acknowledge that they will correct any errors which they become aware of in the specification.

II. The Examiner noted the use of trademarks in the specification and specifically noted two examples of allegedly improper use (SEPHAROSE at page 22, line 21 and Amicon on page 27, line 8). Applicants have reviewed the entire specification for the use of trademarks. Applicants have herein amended the specification to indicate the trademark SEPHAROSE with capitalization. "Amicon" is the actual name of a corporation and is not a trademark in itself.

III. The Abstract stands objected to for the utilization of legal phraseology ("said"). Applicants have herein amended the abstract to remove the legal phraseology ("said").

IV. The Examiner has objected to the specification for the alleged improper incorporation of essential material (at page 33, lines 3-8) into the specification by reference to a foreign application or patent, or to a publication.

According to MPEP 608.01(p), "essential" material is defined as; 1)necessary to describe the invention, 2) necessary to provide an enabling disclosure and 3) necessary to describe the best mode.

"Non-essential" material is defined as material used to indicate the background of the invention and the state of the art. Non-essential material may be incorporated by reference into a specification. Thus, Applicants respectfully submit that the text at page 33, lines 3-8 of the instant specification is a proper incorporation by reference of non-essential material.

Applicants have addressed all of the outstanding objections to the specification in the above remarks and with the amendments to the specification and thus respectfully request that all objections to the specification now be withdrawn.

**Objections to the Claims**

Claims 3-9, 18-28 and 33-35, as originally presented, stand objected to for informality of claim numbering. The Examiner notes that claims 1 and 2 are identified as " Claim 1 and Claim 2" while the other claims of the application are referred to by number only.

Claims 3-9, 18-28 and 33-35 have been canceled and all remaining pending claims are identified using the word "claim" followed by the appropriate number. Thus, a single format is now consistently used for clarity.

Claims 3-9, 18-28 and 33-35, as originally presented, also stand objected to for referring to the biopolymer of claim 1. The Examiner requests the use of "SEQ ID NO:1" in place of the "biopolymer of claim 1".

Claims 3-9, 18-28 and 33-35 have been canceled and none of the remaining pending claims refer to the biopolymer of claim 1.

Accordingly, Applicants have addressed all objections to the claims and respectfully request that all of the above-mentioned objections to the claims now be withdrawn.

**Rejections under 35 USC 112(second paragraph)**

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The Examiner alleges that the term "particularly" as recited in claims 4 and 5 renders the claims vague and indefinite because the claims include elements not actually disclosed, thereby rendering the scope of the claims unascertainable.

Claims 4 and 5 have been canceled and the term "particularly" is not recited in any of the remaining pending claims.

B. The Examiner alleges that the terms "evidencing" and "characterizing" in claims 3-5 are vague and indefinite because it is not clear as to what "evidencing" and "characterizing" encompasses. The Examiner states if the method merely detects congestive heart failure via a biopolymer marker as (defined in the disclosure) it is suggested that the phrases are replaced with "detecting" in order to clarify applicants intended meaning.

Claims 3-5 have been canceled and the terms "evidencing" and "characterizing" are not recited in any of the remaining pending claims.

C. The Examiner alleges that claim 7 is not recited using the proper Markush format. New claim 38 corresponds to canceled claim 7 and now recites proper Markush format.

D. The Examiner alleges that the phrase "at least one analyte thereof" as recited in claims 3-9, 18-28 and 33-35 renders the claims vague and indefinite because it is unclear as to what the phrase is intended to define. Claims 3-9, 18-28 and 33-35 have been canceled and the phrase "at least one analyte thereof" is not recited in any of the remaining pending claims.

E. The Examiner alleges that the term "including" as recited in claims 18, 25 and 33-35 renders the claims vague and indefinite because the term is not clearly defined in the composition/biopolymer of the instant application. Claims 18, 25 and 33-35 have been canceled and the term " including" is not recited in any of the remaining pending claims.

F. The Examiner alleges that the term "regulation" in claim 35 is a relative term which renders the claim indefinite. The term "regulation" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to how the

measurement of the biopolymer marker will further serve to control the absence and/or presence of the aforementioned biopolymer marker or analyte thereof. It is suggested by the Examiner that the claim merely recite detection of the biopolymer.

Claim 35 has been canceled and the term "regulation" is not recited in any of the remaining pending claims.

Accordingly, applicants have now clarified the metes and bounds of the claims and respectfully request that the above-discussed rejections under 35 U.S.C. 112 (second paragraph) be withdrawn.

**Rejection under 35 USC 101**

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 101 because the claimed invention allegedly lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims are now limited to methods and kits using a specific biopolymer marker (SEQ ID NO:1) specifically diagnostic for congestive heart failure. Applicants are not claiming the ability to distinguish between disease states. The instant inventors do not attempt to develop a reference "normal", but rather strive to specify particular markers which are evidentiary of at least one

specific disease state, whereby the presence of said marker serves as a positive indicator of disease (see page 5, lines 7-11 of the instant specification). Applicants claim that the presence of SEQ ID NO:1 is a positive indicator of congestive heart failure. This is a specific, substantial and a credible utility that was established at the time of filing by the data shown in Figure 1. Figure 1 displays a table listing patients having a history of congestive heart failure. All of the patients listed show the presence of SEQ ID NO:1 in their serum.

The Examiner asserts at page 9 of the Office Action mailed April 7, 2003, "The specification also states that the said sequence was highly expressed in congestive heart failure, but undetectable in other tested disease related to Syndrome X, such as overt diabetes and kidney failure. See page 16, lines 9-18 and page 26, line 20 through page 27, line 2." Applicants respectfully disagree with the Examiner. Applicants maintain that the instant specification does not state that SEQ ID NO:1 is highly expressed in congestive heart failure but undetectable in other diseases related to Syndrome X at the pages cited above by the Examiner nor anywhere else in the instant specification.

Additionally, the Examiner cites three patents (inventors; Harrison and Farries) which allegedly relate to the utility of the instant invention; US 5,849,297; US 6,221,657 and US 6,268,485. These patents teach modified human C3 complement proteins which are

capable of forming stable C3 convertases. These modified human C3 complement proteins function to deplete levels of complement pathway proteins and are thus useful as therapeutic agents (not diagnostic agents) in certain clinical situations. Contrary to the Examiner's assertion, none of these patents teach that the modified human C3 complement proteins are diagnostic for myocardial ischemia, frostbite, burns, glomerulonephritis, hemolytic anemia, myasthenia gravis and type II collagen induced arthritis. Nor do any of these patents teach a biopolymer marker sequence diagnostic for congestive heart failure. Applicants respectfully assert that these references have no relevance with regard to the utility of the invention as defined by the pending claims.

As evidenced by the above discussion, Applicants have clarified the specific, substantial and credible utility of the claimed invention and respectfully request that this rejection now be withdrawn.

**Rejections under 35 USC 112(first paragraph)**

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which with it is most nearly connected, to make and/or use the invention.

The Examiner alleges on page 10 of the Office Action mailed on April 7, 2003, that since claims 3-9, 18-28 and 33-35 are not supported by a substantial utility, one skilled in the art would not know how to use the claimed invention without undue experimentation.

As clarified in the above discussion (Rejection Under 35 USC 101), the claimed invention is supported by a substantial utility. Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims are now limited to methods and kits using a specific biopolymer marker (SEQ ID NO:1) specifically diagnostic for congestive heart failure. The presence of SEQ ID NO:1 is a positive indicator of congestive heart failure as shown by the data presented in Figure 1. In light of this substantial utility, Applicants assert that one of ordinary skill in the art when reviewing the instant specification would recognize how to use the claimed sequence (SEQ ID NO:1) as a marker for congestive heart failure. Thus, Applicants respectfully request that this rejection now be withdrawn.

Additionally, claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which with it is most nearly connected, to

make and/or use the invention.

Applicants are currently in the process of preparing a Declaration Under 37 CFR 1.132 in order to provide evidence of the absence of the 1793 dalton biopolymer marker(SEQ ID NO:1) in normal (non-diseased) human sera and will forward this Declaration to the Examiner as soon as it is complete. Applicants will further address this rejection under U.S.C. 112, first paragraph at the time the Declaration is submitted.

**Rejection under 35 USC 102(b)**

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Harrison *et al.* (US 5,849,297).

Harrison *et al.* teach modified human C3 complement proteins which are capable of forming stable C3 convertases. These modified human C3 complement proteins function to deplete levels of complement pathway proteins and are thus useful as therapeutic agents. No where in the patent does Harrison *et al.* teach that SEQ ID NO:1 (as disclosed by Harrison *et al.*) is useful for disease detection or evaluation. SEQ ID NO:1 disclosed in Harrison *et al.* represents 1663 amino acid residues of human C3 complement protein. SEQ ID NO:1 as disclosed in the instant application represents 15 amino acid residues of human C3 complement protein. The 15 amino acid residue SEQ ID NO:1 of the instant invention is identical to

a portion of SEQ ID NO:1 as disclosed by Harrison *et al.*

Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims identify a specific peptide (SEQ ID NO:1) with a specific function (diagnostic for congestive heart failure (CHF)). Harrison *et al.* do not teach that SEQ ID NO:1 (1663 amino acid residues of human C3 complement protein) or any portion thereof is diagnostic for congestive heart failure (CHF).

Accordingly, Applicants respectfully submit that the claims, as instantly presented, now distinguish over the compositions taught by Harrison *et al.* and respectfully request that this rejection be withdrawn.

**Rejections under 35 USC 102 (a) and (e)**

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 102(a) and (e) as allegedly being anticipated by Harrison *et al.* (US 6,221,657).

Harrison *et al.* teach modified human C3 complement proteins which are capable of forming stable C3 convertases. These modified human C3 complement proteins function to deplete levels of complement pathway proteins and are thus useful as therapeutic agents. No where in the patent does Harrison *et al.* teach that SEQ ID NO:1 (as disclosed by Harrison *et al.*) is useful for disease detection or evaluation. SEQ ID NO:1 disclosed in Harrison *et al.* represents 1663 amino acid residues of human C3 complement protein.

SEQ ID NO:1 as disclosed in the instant application represents 15 amino acid residues of human C3 complement protein. The 15 amino acid residue SEQ ID NO:1 of the instant invention is identical to a portion of SEQ ID NO:1 as disclosed by Harrison *et al.*

Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims identify a specific peptide (SEQ ID NO:1) with a specific function (diagnostic for congestive heart failure (CHF)). Harrison *et al.* do not teach that SEQ ID NO:1 (1663 amino acid residues of human C3 complement protein) or any portion thereof is diagnostic for congestive heart failure (CHF).

Accordingly, Applicants respectfully submit that the claims, as instantly presented, now distinguish over the compositions taught by Harrison *et al.* and respectfully request that this rejection be withdrawn.

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Farries *et al.* (US 6,268,485).

Farries *et al.* teach modified human C3 complement proteins which are capable of forming down-regulation resistant C3 convertases. These modified human C3 complement proteins function to deplete levels of complement pathway proteins and are thus useful as therapeutic agents. No where in the patent does Farries *et al.* teach that SEQ ID NO:22 (as disclosed by Farries *et al.*) is

useful for disease detection or evaluation. SEQ ID NO:22 disclosed in Farries *et al.* represents 1663 amino acid residues of human C3 complement protein. SEQ ID NO:1 as disclosed in the instant application represents 15 amino acid residues of human C3 complement protein. The 15 amino acid residue SEQ ID NO:1 of the instant invention is identical to a portion of SEQ ID NO:22 as disclosed by Farries *et al.*

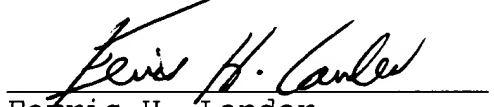
Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims identify a specific peptide (SEQ ID NO:1) with a specific function (diagnostic for congestive heart failure (CHF)). Farries *et al.* do not teach that SEQ ID NO:22 (1663 amino acid residues of human C3 complement protein) or any portion thereof is diagnostic for congestive heart failure (CHF).

Accordingly, Applicants respectfully submit that the claims, as instantly presented, now distinguish over the compositions taught by Farries *et al.* and respectfully request that this rejection be withdrawn.

## CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



Ferris H. Lander
Registration # 43,377

McHale & Slavin, P.A.
2855 PGA Boulevard
Palm Beach Gardens, FL 33410
(561) 625-6575 (Voice)
(561) 625-6572 (Fax)

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